

Frequently Asked Questions (FAQs)

➤ **What is Bioclynse Wound Irrigation Solution?**

Bioclynse Wound Irrigation Solution (WIS) is a copper - iodine complex-based solution that is topically applied to wound areas. The clear product generates free iodine (I₂) locally on the wound in a concentration of up to 250 parts per million (ppm). Free iodine acts as a powerful preservative agent of broad antimicrobial spectrum that maintains self-sterility and allows for effective wound cleaning and is not intended to provide therapeutic benefit.

Bioclynse WIS is a medical device 510(k)-cleared by the FDA (K181428)¹. The subject device is a wound management and cleansing solution that is intended for use by healthcare professionals for cleansing, irrigating, moistening and debriding to remove wound debris from acute and chronic dermal lesions that are partial or full thickness wounds such as 1st and 2nd degree burns, stage I - IV pressure ulcers, diabetic ulcers, stasis ulcers, abrasions and minor skin irritations, post-surgical wounds, grafted and donor sites, in addition to moistening and lubricating absorbent wound dressings (e.g. gauze). The mechanical action of fluid moving across the wound provides for the mechanism of action and aids in the removal of foreign objects such as dirt and debris¹.

Bioclynse WIS technology serves as a platform for several wound management applications, including the irrigation of post-surgical wounds by incorporating a hanger system and septum cap that work in tandem with a vented spike irrigation set for controlled application to affected areas.

➤ **What is the copper-iodine complex technology behind Bioclynse and how does this help to reduce contamination, biofilm and bacterial burden on the wound bed?**

The mechanical action of fluid moving across the wound aids in the removal of contamination or foreign objects such as dirt and debris. Additionally, the powerful yet safe iodine-copper complex contained in Bioclynse WIS as a preservative allows the release of a controlled amount of free iodine (up to 250 ppm), which along with copper ions, produces a synergic effect that improves the cleansing, irrigating, and debriding effect on wounds.

Although iodine is not intended to provide therapeutic benefit with Bioclynse use, it is a very well-established antiseptic that has been in use for more than 150 years. It is one of the most widely accepted antimicrobials in the world with broad spectrum of antimicrobial activity, rapidly inhibiting bacteria, yeasts, molds, protozoa and viruses and no known acquired resistance. Its mechanism of action works in two ways: (1) Penetration into the cell wall of the microorganism, causing blocking of the hydrogen bond which results in damage to the phospholipid cell membrane; (2) Damage and denaturing of the proteins, nucleotides and fatty acids, leading to rapid cell death by binding to amine and sulphhydryl groups².

Additionally, numerous studies worldwide have shown that copper ions, in controlled doses, have unique properties to promote better wound healing such as: formation of new blood vessels for

tissue regeneration³, anti-inflammatory properties⁴, and weakening of biofilms to allow a better antimicrobial effect^{5,6}.

➤ **What are the benefits of Bioclynse?**

- Extremely high efficacy: preservative system with 99.999% kill rate against bacteria, viruses and fungi. Highly effective and sustained microbial control up to 3 days.
- Effective against biofilms
- No known microbial resistance
- Safe / non-irritating / non-toxic / non-sensitizing
- Tissue friendly / bio-compatible
- Non-staining / colorless / odorless
- Balanced pH for wound healing
- No rinsing, mixing or dilution required
- Wound odor control
- Environmentally friendly
- Store at room temperature

➤ **How effective is Bioclynse?**

The antimicrobial properties of this iodine-copper technology as a preservative in solution have been assessed against bacterial pathogens commonly associated with wound infections (ESKAPE pathogens), including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecalis* (VRE), *Cutibacterium acnes* and *Pseudomonas aeruginosa*. GLP testing has shown that Bioclynse WIS formula can reduce bacterial and fungal burden by >99.999% (5 log reduction) for up to 3 days⁷. An *in vivo* anti-biofilm model showed 2.0-2.5 log reduction (vs. Standard of Care <1.0 log reduction)⁸.

➤ **What are the main differences between Bioclynse WIS technology and other iodine-based solutions?**

One of the first antiseptic preparations of iodine was Lugol's solution in 1829. This was a strong aqueous solution of iodine and potassium iodide in ethanol and was used as an antiseptic to treat wounds. However, the high concentration of iodine (up to 100,000 ppm) caused pain, irritation, destruction of mucosa as well as major concerns regarding cytotoxicity, systemic absorption, and delayed wound healing².

In 1956 Povidone-Iodine (PVP-I) was developed in an attempt to reduce these clinical concerns but the concentrations of iodine were still high (about 10,000 ppm) and so the problems associated with iodine were not completely diminished. Betadine is a tradename for PVP-I, which is currently available as an antiseptic to treat minor cuts, scrapes or burns only. This formula is a 10% solution which claims 1% (10,000 ppm) of available iodine. The available free iodine depends on the

formulation, concentration and temperature as it is a dependent equilibrium of povidone-bound iodine to free iodine⁹.

In vitro studies (IJS, 2017)¹⁰ have suggested that PVP-I has a cytotoxic effect but that dilution to 10% (1,000 ppm) may reduce the inhibition of the granulation and epithelialization processes, therefore the general protocol observed when using diluted PVP-I involves a very short application time followed by an immediate flush with saline. Effects of this dilution and saline flushing have not been tested or proven with respect to the resulting cytotoxicity or antimicrobial profile.

As free iodine is considered one of the most efficacious broad spectrum topical antiseptics, with no known resistance, the most optimal approach would be a complex with low concentration of iodine, but that can release highly effective levels of free iodine against wound pathogens and biofilms, with no toxicity or delayed wound healing.

In 2012, Clyra Medical initiated the development of such product. After many years of formulation work and efficacy testing, the resulting Bioclynse WIS provides a unique stable copper-iodine complex as a preservative in solution with up to 250 ppm of free iodine. The product has a very safe and non-toxic profile yet maintains the efficacy of its iodine predecessors that incorporate iodine at 10,000 – 100,000 ppm.

➤ **What is the effectiveness period of Bioclynse WIS after one application?**

Bioclynse WIS by means of its unique stable copper-iodine complex acting as a preservative in solution reaches more than 5 log reduction of burden load for all ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter species*), other bacteria strains and fungus (*Candida albicans* and *Candida tropicalis*) with sustained activity up to 3 days.

The preparation (Bioclynse WIS) containing the copper-iodine complex based preservative has also been tested against biofilm using an *in vivo* porcine model and exhibited a 2.0-2.5 log reduction against mature biofilm.

➤ **What type of wounds can be treated with Clyra WIS?**

Bioclynse WIS is intended for cleansing, irrigating, moistening and debriding to remove wound debris from acute and chronic dermal lesions that are partial or full thickness wounds such as 1st and 2nd degree burns, stage I - IV pressure ulcers, diabetic ulcers, stasis ulcers, abrasions and minor skin irritations, post-surgical wounds, grafted and donor sites, in addition to moistening and lubricating absorbent wound dressings.

➤ **Is Bioclynse WIS stable and safe for wound management?**

Yes, as part of demonstrating safety and effectiveness of Clyra WIS to get the 510(k) clearance from the FDA, Clyra Medical Technologies Inc. completed GLP biocompatibility testing (ISO 10993) to establish the safety of Bioclynse WIS for its intended use.

- Cytotoxicity assay (ISO 10993-5:2009)¹¹.

- Porcine wound healing study (pathology and histology studies completed)¹².
- Sensitization test (ISO 10993-10:2010)¹³.
- Direct primary skin irritation test - ISO abraded method (ISO 10993-10:2010)¹⁴.
- Material medicated pyrogenicity¹⁵.
- Chemical characterization¹⁶ and toxicological risk assessment for systemic toxicity¹⁷.
- Antimicrobial Effectiveness Test (AET) (USP<51>): Bioclynse WIS was evaluated for preservative activity in compliance with USP Antimicrobial Effectiveness Test<51>. Exposure to Bioclynse WIS caused an inhibition in *Pseudomonas aeruginosa*, *E. coli*, *Staphylococcus aureus*, *Candida albicans*, and *Aspergillus brasiliensis*¹⁸.
- Stability Testing: Bioclynse WIS was stable in composition, appearance, pH and self-sterile capacity (microbiological evaluation) for 2+ years, when stored unopened at ambient temperature, in accordance with the manufacturer's recommendations¹⁷. Clyra WIS was also stable at 40°C up to 6+ months¹⁹.

From the above testing, it was concluded that Bioclynse WIS is host-tissue friendly, non-cytotoxic, non-irritant, non-pyrogenic, non-sensitizing, self-sterile and stable in its physico-chemical properties for 2+ years, as well as there is not associated risk for chronic and sub-chronic systemic toxicity (prolonged contact >24 hours < 30 days) or delayed wound healing up to 28 days.

➤ **Does Bioclynse WIS have any warning or contraindication?**

- For external use only.
- Not for injection, IV or ophthalmic use.
- Do not use if there is a history of allergy to any of the ingredients.
- The product is contraindicated for use in patients with Wilson's disease.
- Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

➤ **How to use Bioclynse WIS?**

- For general use on wounds, apply the Bioclynse WIS directly on the wound bed to flush away dirt and debris and ensure the wound is thoroughly cleaned.
- Bioclynse WIS may be used with a vented spike irrigation set prior to hanging for application.
- Bioclynse WIS may be used with pulse lavage, ultrasonic debridement and negative pressure wound therapy.
- If dressing is used, saturate it with Bioclynse WIS and apply directly over the wound.
- For single use only.
- No rinsing required afterwards.

For more details, please see the Instructions of Use provided with the product.

➤ **What is the frequency of use for Bioclynse WIS?**

Can be used as prescribed for routine wound irrigation and dressing change applications.

➤ **Is it necessary to rinse with saline or water after irrigation with Bioclynse WIS?**

No, Bioclynse WIS is safe for prolonged use with no rinsing or dilution required after application.

➤ **Can Bioclynse WIS be used as a complement of other wound care therapies?**

Bioclynse WIS is designed for a synergistic approach to wound bed preparation and management, and is compatible with pulse lavage, ultrasonic debridement and negative pressure wound therapy.

➤ **Does Bioclynse require any special handling, storage or disposal requirement?**

Handling: Non-irritating, non-toxic, and non-sensitizing. No special handling precautions required.

Storage Conditions: Store at 15 – 30 °C (59-86 °F). Avoid excessive heat.

Disposal: Dispose of the bottle and solution after expiration date. No special disposal considerations are required.

➤ **What is the shelf life of Bioclynse WIS prior and after opening?**

Bioclynse WIS can be stored unopened at room temperature until two years (shelf life). Once opened should be discarded in 30 days.

➤ **What is the package configuration?**

Clyra WIS is available in 8oz, 16oz, 32 oz and 48oz bottles with septum cap for instillation. Pack of 6 bottles.

References

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